WEST Search History

DATE: Wednesday, September 24, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L6	L5 and motor neuron	5	L6
L5	L4 and c-myc	18	L5
L4	L3 and (neurofilament L or NF-L)	55	L4
L3	L2 and transgenic mouse	713	L3
L2	L1 and transgenic	1140	L2
L1	neurofilament	1774	L1

END OF SEARCH HISTORY

9/24/03
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Set	Items	Description
S1	33016	NEUROFILAMENT
S2	453	S1 AND TRANSGENIC(W)MOUSE
S3	1	S2 AND C-MYC
S4	16	S2 AND (NEUROFILAMENT(W)L OR NF-L)
S5	16	RD (unique items)
S6	6	S5 AND MOTOR(W)NEURON

?t 6/3,ab/1-6
>>>No matching display code(s) found in file(s): 65, 135

Dialog
file: medicine
9/24/03
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6/3,AB/1 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05824197 Genuine Article#: XA144 Number of References: 37
Title: Role of neurofilaments in amyotrophic lateral sclerosis (ABSTRACT AVAILABLE)
Author(s): Julien JP (REPRINT)
Corporate Source: MCGILL UNIV,HOP GEN MONTREAL, INST RECH, CTR RECH NEUROSCI, 1650 CEDAR/MONTREAL/PQ H3G 1A4/CANADA/ (REPRINT)
Journal: M S-MEDECINE SCIENCES, 1997, V13, N4 (APR), P549-556
ISSN: 0767-0974 Publication date: 19970400
Publisher: JOHN LIBBEY EUROTEXT LTD, 127 AVE DE LA REPUBLIQUE, 92120 MONTROUGE, FRANCE
Language: French Document Type: ARTICLE
Abstract: Amyotrophic lateral sclerosis (ALS) is a late-onset degenerative disease of motor neurons characterized by the abnormal accumulation of neurofilaments in perikarya and proximal axons. Until recently, the depositions of neurofilaments observed in neurodegenerative disorders were widely considered a secondary effect of neuronal dysfunction. However, recent studies with **transgenic mouse** models demonstrated that **neurofilament** accumulations can play a causative role in **motor neuron** disease by disrupting axonal transport. The hypothesis that neurofilaments contribute to ALS pathogenesis is also supported by the discovery of mutations in the gene coding for the **neurofilament** heavy subunit (NF-H) from some ALS cases. A link may exist between neurofilaments and the abnormal activity of the superoxide dismutase (SOD1) responsible for similar to 2% of ALS cases. The presence of abnormal **neurofilament** accumulations in familial ALS cases with different SOD1 mutations and in transgenic mice expressing SOD1 mutants suggest that neurofilaments could be a target of toxicity induced by SOD1 mutants.

6/3,AB/2 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04593902 Genuine Article#: TV592 Number of References: 45
Title: A ROLE FOR NEUROFILAMENTS IN THE PATHOGENESIS OF AMYOTROPHIC-LATERAL-SCLEROSIS (Abstract Available)
Author(s): JULIEN JP
Corporate Source: MONTREAL GEN HOSP,RES INST,NEUROSCI RES CTR,1650 CEDAR AVE/MONTREAL/PQ H3G 1A4/CANADA/
Journal: BIOCHEMISTRY AND CELL BIOLOGY-BIOCHIMIE ET BIOLOGIE CELLULAIRE, 1995, V73, N9-10 (SEP-OCT), P593-597
ISSN: 0829-8211
Language: ENGLISH Document Type: REVIEW
Abstract: Amyotrophic lateral sclerosis (ALS) is a late-onset degenerative disease of motor neurons, characterized by abnormal accumulation of neurofilaments (NFs) in perikarya and proximal axons. Two lines of evidence suggest that **neurofilament** accumulation can play a crucial role in ALS pathogenesis. First, **transgenic mouse** models overexpressing NF proteins were found to develop **motor neuron** degeneration and, second, variant alleles of the NF heavy-subunit

(NF-H) gene have been found in some human ALS patients. Our axonal transport studies with transgenic mice overexpressing the human NF-H gene, a model of ALS, revealed defects of intracellular transport not only for **neurofilament** proteins but also for other cytoskeletal proteins and organelles such as mitochondria. Therefore, we propose that **neurofilament** accumulation in mice causes neurodegeneration by disrupting axonal transport, a mechanism that may account for the pathogenesis of ALS.

6/3,AB/3 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04143806 Genuine Article#: RH249 Number of References: 25
Title: ABNORMAL PERIKARYAL ACCUMULATION OF NEUROFILAMENT **LIGHT PROTEIN IN THE BRAIN OF MICE TRANSGENIC FOR THE HUMAN PROTEIN - SEQUENCE OF POSTNATAL-DEVELOPMENT** (Abstract Available)
Author(s): MA D; DESCARRIES L; JULIEN JP; DOUCET G
Corporate Source: UNIV MONTREAL,FAC MED,DEPT PATHOL/MONTREAL/PQ H3C 3J7/CANADA/; UNIV MONTREAL,FAC MED,DEPT PATHOL/MONTREAL/PQ H3C 3J7/CANADA/; UNIV MONTREAL,FAC MED,CTR RECH SCI NEUROL/MONTREAL/PQ H3C 3J7/CANADA/; MONTREAL GEN HOSP,RES INST,CTR RES NEUROSCI/MONTREAL/PQ H3G 1A4/CANADA/
Journal: NEUROSCIENCE, 1995, V68, N1 (SEP), P135-149
ISSN: 0306-4522
Language: ENGLISH Document Type: ARTICLE
Abstract: Adult mice transgenic for the human form of **neurofilament** light protein display abnormal perikaryal immunoreactivity for this protein in many regions of the CNS and notably the thalamus. To determine the sequence of development of these anomalies, we have compared normal and transgenic mice of different postnatal ages (P0-P70), using immunocytochemistry with primary antibodies recognizing both murine and human sequence of **neurofilament** light protein (NR-4) or the human form only (DP5-1-12). In normal mouse brainstem, several nuclei displayed immunoreactive perikarya at P0. The number of these perikarya culminated at P10, followed by a general decrease, some nuclei having lost all perikaryal immunostaining in adults. In **transgenic mouse** brainstem, the distribution of perikaryal immunoreactivity already resembled at P0 that of P10 in normal mouse, and remained unchanged in adults. Differences between normal and transgenic mice were even more pronounced in the forebrain. Some nuclei of normal mouse basal forebrain that were weakly immunopositive at P10 or P20, but no longer in adults, were already labeled at P0 and remained so or became more intense at later stages in transgenic mice. In the thalamus of normal mouse, perikaryal labeling was faint, confined to a few nuclei, and detected only transiently at P10, whereas in transgenics, it was already observed in some nuclei at P0, increased in intensity and extended to other nuclei at P10, and persisted thereafter. Strongly immunoreactive, inflated perikarya with excentric nuclei were prominent in these thalamic nuclei at P20, and even larger in size at P70. In the cerebral cortex of normal mice, layers II-III and layer V of many cytoarchitectonic areas showed immunoreactive cell bodies at P10, a distribution which became gradually restricted to the parietal cortex in adults. In transgenic mice, immunopositive cortical cell bodies were first detected at P3, filled layers II-III of numerous cortical areas at P10, and then rapidly decreased in number to approach the adult pattern at P20. In the cortex as well as thalamus of P10 transgenic mice, differences between the patterns of cellular staining with clones NR4 and DP5-1-12 antibodies indicated that both the murine and human proteins were accumulated in these neurons.

Thus, **neurofilament** light protein accumulation in the **transgenic mouse** brain generally involved neurons displaying perikaryal immunoreactivity for the protein at least at some point during normal postnatal development. Yet, the most remarkable perikaryal accumulations of **neurofilament** light protein were found in two

regions of the forebrain, the thalamus and cerebral cortex, known as **neurofilament** -poor in normal mouse and where, presumably, neuronal metabolism could not cope with higher rates of synthesis of this protein. Further studies will be needed to determine the fate of the neurons afflicted by such abnormal accumulations of **neurofilament** light protein at different stages of their development or maturity.

6/3,AB/4 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03581599 Genuine Article#: PP533 Number of References: 78
Title: A MUTANT NEUROFILAMENT **SUBUNIT CAUSES MASSIVE, SELECTIVE** MOTOR - NEURON **DEATH - IMPLICATIONS FOR THE PATHOGENESIS OF HUMAN** MOTOR - NEURON **DISEASE** (Abstract Available)
Author(s): LEE MK; MARSZALEK JR; CLEVELAND DW
Corporate Source: JOHNS HOPKINS UNIV,SCH MED,DEPT BIOL CHEM/BALTIMORE//MD/21205; JOHNS HOPKINS UNIV,SCH MED,DEPT NEUROSCI/BALTIMORE//MD/21205
Journal: NEURON, 1994, V13, N4 (OCT), P975-988
ISSN: 0896-6273
Language: ENGLISH Document Type: ARTICLE
Abstract: A direct role of aberrant **neurofilament** accumulation in the etiology of human **motor neuron** diseases, including amyotrophic lateral sclerosis, is suggested by the presence of abnormal accumulations of neurofilaments as an early hallmark of the pathogenic process. Furthermore, forcing increased expression of **neurofilament** subunits in **transgenic mouse** models leads to **motor neuron** dysfunction, albeit without the widespread **motor neuron** death typical of human disease. We now show that accumulation of a modest level of a point mutant in the smallest **neurofilament** subunit (NF-L) causes massive, selective degeneration of spinal motor neurons accompanied by abnormal accumulations of neurofilaments and severe neurogenic atrophy of skeletal muscles. As in hu man disease, sensory neurons show only a modest level of degenerative changes. Thus, **neurofilament** mutations can cause selective **motor neuron** death, and neurofilamentous abnormalities may be a common toxic intermediate that significantly contributes to the **motor neuron** death in human disease.

6/3,AB/5 (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text

03506108 H.W. WILSON RECORD NUMBER: BGSI97006108
The cytoskeleton and disease: genetic disorders of intermediate filaments.
Fuchs, Elaine
Annual Review of Genetics (Annu Rev Genet) v. 30 ('96) p. 197-231
SPECIAL FEATURES: bibl il ISSN: 0066-4197
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: 16346

ABSTRACT: The current understanding of the genetic disorders associated with the cytoskeletons of intermediate filaments (IFs) is discussed. IF proteins contain highly conserved sequences that are particularly important in IF network formation and filament assembly. Epidermal cells produce extensive networks of keratins, and a number of diseases associated with keratin gene defects or abnormal keratin IF networks have recently been identified. These diseases include epidermolysis bullosa simplex, epidermolytic hyperkeratosis (EH), epidermal nevi of the EH type, palmoplantar keratoderma, pachyonychya congenita, and white sponge nevus. Several neurological disorders and some forms of congenital myopathies also appear to be caused by genetic disorders of IFs. The study of these diseases has revealed the importance of keratins, and perhaps other IFs, in

maintaining the mechanical integrity of cells.

6/3,AB/6 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

137274036 CA: 137(19)274036x PATENT
Compositions and methods for screening for factors inhibiting motor neuron degeneration using neurofilament light chain gene transgenic mouse
INVENTOR(AUTHOR): Schlaepfer, William W.; Canete-Soler, Rafaela
LOCATION: USA
PATENT: U.S. Pat. Appl. Publ. ; US 20020142338 A1 DATE: 20021003
APPLICATION: US 82032 (20020221) *US PV117007 (19990125) *US 489979 (20000121) *US 994420 (20011127)
PAGES: 13 pp., Cont.-in-part of U.S. Ser. No. 944,420. CODEN: USXXCO
LANGUAGE: English CLASS: 435006000; C12Q-001/68A; C12N-009/64B
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